Expression of migration-related genes is progressively upregulated in murine Lineage-Sca-1+c-Kit+ population from the fetal to adult stages of development.

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Authors: Jesus Ciriza, Marcos E Garcia-Ojeda

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Public Summary:
Abstract Introduction: Hematopoietic stem cells (HSCs) follow a genetically programmed pattern of migration during development. Extracellular matrix and adhesion molecules, as well as chemokines and their receptors, are important in adult HSC migration. However, little is known about the role these molecules play at earlier developmental stages. Methods: We have analyzed by quantitative polymerase chain reaction (qPCR) array the expression pattern of extracellular matrix and adhesion molecules as well as chemokines and chemokine receptors in Lineage-Sca-1+c-Kit+ (LSK) cells at different stages of development, in order to characterize the role played by these molecules in LSK. Data were represented by volcano plots to show the differences in expression pattern at the time points studied. Results: Our results show marked changes in the expression pattern of extracellular matrix, adhesion molecules, chemokines and their receptors with developmental age, particularly in later stages of development. Ten molecules were significantly increased among the LSK populations studied. Our screen identified the upregulation of Col4a1, as well as molecules involved in its degradation (Mmp2, Timp2), with development. Other genes identified were Sell, Tgfbi, and Entpd1. Furthermore, we show that the expression of the chemokines Ccl4, Ccl9, Il18 and the chemokine receptor Cxcr4 increases in LSK cells during development. Conclusions: Several genes are upregulated in the LSK population in their transition to the bone marrow microenvironment, increasing at later stages of development. This gene pattern should be emulated by embryonic stem cell-derived hematopoietic progenitors in order to improve their properties for clinical applications such as engraftment.

Scientific Abstract:
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